APPLICANTS: Bacus, et al
U.S.S.N.: 10/735,118

LISTING OF CLAIMS

Claims 1-83. (Cancelled)

Claim 84. (Previously Amended) A method for identifying a HER-2 over-expressing mammalian tumor that is likely to respond to a HER-2 directed therapy, the method comprising the steps of:

(i) assaying a sample obtained from the mammalian tumor to detect a pattern of:

(a) phosphorylation of an S6 ribosomal polypeptide;

(b) expression of an IGFR (Insulin-like Growth Factor Receptor) polypeptide; and optionally

(c) expression of a NDF (Heregulin) polypeptide; and

(ii) comparing said pattern to a pattern detected in a sample obtained from a non-tumor tissue or cell sample, wherein a change in the detected pattern identifies said mammalian tumor as likely to respond to a HER-2 directed therapy.

Claim 85. (Previously Amended) The method of claim 84, wherein the detected pattern is increased phosphorylation of S6 ribosomal polypeptide, accompanied by decreased expression of IGFR polypeptide in the mammalian tumor as compared to said non-tumor tissue or cell sample, wherein said pattern identifies said tumor as likely to respond to a HER-2 directed therapy.

Claim 86. (Previously Presented) The method of claim 84, wherein the detected pattern is increased expression of NDF polypeptide, accompanied by increased phosphorylation of S6 ribosomal polypeptide and decreased expression of IGFR polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as likely to respond to a HER-2 directed therapy.

Claim 87. (Previously Amended) The method of claim 84, wherein the detected pattern of phosphorylation of S6 ribosomal polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated serine residue at position 235 in SEQ ID NO: 2.

Claim 88. (Previously Amended) The method of claim 84, wherein said mammalian tumor is a breast tumor.

Claim 89. (Previously Amended) A method for identifying a HER-2 over-expressing mammalian tumor that is likely to respond to a HER-2 directed therapy, the method comprising the steps of:

(i) assaying a sample obtained from the mammalian tumor to detect a pattern of expression or phosphorylation of two or more polypeptides selected from the group consisting of:

(a) expression of an IGFR (Insulin-like Growth Factor Receptor) polypeptide;

(b) phosphorylation of an S6 ribosomal polypeptide;

(c) expression of a NDF (Heregulin) polypeptide;

(d) expression of an EGFR (Epidermal Growth Factor Receptor) polypeptide;

(e) phosphorylation of an AKT polypeptide; and

(f) phosphorylation of an ERK polypeptide; to establish a first detected pattern and

(ii) comparing said pattern to a pattern detected in a sample obtained from a non-tumor tissue or cell sample, wherein a change in the detected pattern identifies said mammalian tumor as likely to respond to a HER-2 directed therapy.

Claim 90. (Previously Presented) The method of claim 89, wherein the detected pattern is increased expression of NDF polypeptide, accompanied by increased phosphorylation of S6 ribosomal polypeptide and decreased expression of IGFR polypeptide in the

mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as likely to respond to a HER-2 directed therapy.

Claim 91. (Previously Presented) The method of claim 89, wherein the detected pattern is decreased expression of NDF polypeptide, accompanied by increased expression of IGFR polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as not likely to respond to a HER-2 directed therapy.

Claim 92. (Previously Presented) The method of claim 89, wherein the detected pattern is decreased expression of NDF polypeptide, accompanied by a decrease in phosphorylation of the S6 ribosomal polypeptide and decreased expression of IGFR polypeptide and in the mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as not likely to respond to a HER-2 directed therapy.

Claim 93. (Previously Presented) The method of claim 89, wherein the detected pattern is decreased expression of NDF polypeptide, accompanied by decreased expression of EGFR polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as not likely to respond to a HER-2 directed therapy.

Claim 94. (Previously Presented) The method of claim 89, wherein the detected pattern is decreased expression of NDF polypeptide, accompanied by increased phosphorylation of ERK polypeptide and increased expression of EGFR polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as not likely to respond to a HER-2 directed therapy.

Claim 95. (Previously Presented) The method of claim 89, wherein the detected pattern is increased expression of NDF polypeptide, accompanied by increased phosphorylation of

ERK polypeptide and decreased expression of EGFR polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as not likely to respond to a HER-2 directed therapy.

Claim 96. (Previously Presented) The method of claim 89, wherein the detected pattern is decreased expression of EGFR polypeptide, accompanied by increased phosphorylation of ERK polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as not likely to respond to a HER-2 directed therapy.

Claim 97. (Previously Presented) The method of claim 89, wherein the detected pattern is decreased expression of EGFR polypeptide, accompanied by decreased phosphorylation of AKT polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as not likely to respond to a HER-2 directed therapy.

Claim 98. (Previously Presented) The method of claim 89, wherein the detected pattern is increased expression of IGFR polypeptide, accompanied by increased phosphorylation of S6 ribosomal polypeptide in the mammalian tumor as compared to a non-tumor tissue or cell sample, wherein said pattern identifies said tumor as not likely to respond to a HER-2 directed therapy.

Claim 99. (Previously Presented) The method of claim 89, wherein the detected pattern of expression and phosphorylation or both expression and phosphorylation is determined subsequent to contacting the sample obtained from the mammalian tumor with a HER-2 directed therapy.

Claim 100. (Previously Presented) The method of claim 89, wherein the HER2-directed therapy comprises rhuMAb HER-2.

Claim 101. (Previously Amended) The method of claim 89, wherein the detected pattern of expression or phosphorylation of one or a plurality of polypeptides (a) through (f) of steps (i) and (ii) are determined using an antibody, a nucleic acid probe, and/or a peptide probe.

Claim 102. (Previously Presented) The method of claim 89, wherein the detected pattern of phosphorylated AKT polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated serine residue at position 473 in SEQ ID NO: 1.

Claim 103. (Previously Presented) The method of claim 89, wherein the detected pattern of phosphorylated S6 ribosomal polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated serine residue at position 235 in SEQ ID NO: 2.

Claim 104. (Previously Presented) The method of claim 89, wherein the detected pattern of phosphorylated ERK polypeptide is determined using an antibody specific for an epitope comprising a phosphorylated threonine residue at 202 or a phosphorylated serine residue at position 204 in SEQ ID NO: 3.

Claim 105. (Previously Presented) The method of claim 89, wherein the sample obtained from the mammalian tumor is a paraffin-embedded biopsy sample.

Claim 106. (Previously Presented) The method of claim 89, wherein the mammalian tumor is identified as overexpressing HER-2 using an antibody that binds HER-2 polypeptide.

Claim 107. (Previously Presented) The method of claim 89, wherein said mammalian tumor is a breast tumor.

Claim 108. (Currently Amended) A kit for identifying a mammalian tumor that is likely to respond to a HER2-directed therapy, the kit comprising:

(a) an antibody that binds HER-2 polypeptide, and one or more of the following:

(b) an antibody that binds phosphorylated AKT polypeptide;

(c) an antibody that binds phosphorylated S6 ribosomal polypeptide;

(d) an antibody that binds EGFR polypeptide;

(e) an antibody that binds IGFR ~~HER2~~ polypeptide;

(f) an antibody that binds NDF polypeptide; and

(g) an antibody that binds phosphorylated ERK polypeptide.

Claim 109. (Previously Presented) The kit of claim 108, wherein the antibody of (b) is specific for AKT polypeptide having a phosphorylated serine residue at position 473 in SEQ ID NO: 1; wherein the antibody of (c) is specific for S6 ribosomal polypeptide having a phosphorylated serine residue at position 235 in SEQ ID NO: 2; and/or antibody of (f) is specific for EKT polypeptide having a phosphorylated threonine residue at position 202 and a phosphorylated tyrosine at position 204 in SEQ ID NO: 3.

Claim 110. (Previously Presented) The kit of claim 108, wherein the kit further comprises at least one secondary antibody that binds to an antibody of subpart (a) through (g).

Claim 111. (Previously Presented) The method of claim 84, wherein the HER2-directed therapy comprises rhuMAb HER-2.

Claim 112. (Previously Presented) The method of claim 84, wherein the sample obtained from the mammalian tumor is a paraffin-embedded biopsy sample.

Claim 113. (Previously Presented) The method of claim 84, wherein the mammalian tumor is identified as overexpressing HER-2 using an antibody that binds HER-2 polypeptide.